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Pharmacology, Biochemistry and Behavior 77 (2004) 21–28
PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR
www.elsevier.com/locate/pharmbiochembeh

Effects of nicotine on elevated plus maze and locomotor activity in male and female adolescent and adult rats☆

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Received 6 May 2003; received in revised form 26 August 2003; accepted 16 September 2003

Abstract

Over 4500 adolescents start smoking every day in the United States. Of these, one-third will die prematurely from smoking-related diseases. The current experiment examined the effects of repeated-acute nicotine administration (saline, 0.1, 0.5, or 1.0 mg/kg daily) on elevated plus maze (EPM) and locomotor behaviors of 160 adolescent and adult male and female Sprague–Dawley rats. Nicotine's effects depended on age and sex of animal. On the EPM, nicotine exerted anxiolytic effects (increased percentage of time in the open arms) in adolescent males, but exerted anxiogenic effects (decreased percentage of time in the open arms) in adolescent females and in adult males and females. For adults, peak locomotor activity occurred at the 0.5-mg/kg dosage, and the 1.0-mg/kg dosage reduced activity below the saline level on Day 1 and below the 0.5-mg/kg level on Days 1, 3, and 5. For adolescents, peak locomotor activity occurred at the 1.0-mg/kg dosage and there were no activity-depressant effects. These findings suggest there are age differences in sensitivity to nicotine that may affect vulnerability to long-term tobacco use.

Keywords: Nicotine; Elevated plus maze; Nicotine; Locomotion; Anxiety; Adolescence; Sprague–Dawley

1. Introduction

Despite the well-known health effects of tobacco and the addictive liability of nicotine, over 4500 adolescents start smoking every day in the United States (Gilpin et al., 1999; American Lung Association, 2002). It is estimated that over 6 million children eventually will die prematurely from smoking-related diseases (CDC, 1998; American Lung Association, 2002). Further, of current adult smokers, 90% report initiation of smoking in adolescence (Dappen et al., 1996; Chassin et al., 1996; U.S. Department of Health and Human Services, 1989). Together, these reports suggest that adolescence may be a critical vulnerable period for the initiation and maintenance of tobacco use. Understanding the factors contributing to this vulnerability, therefore, may be the key to preventing adolescent smoking.

It is possible that an important reason for tobacco use by adolescents is one that has not been thoroughly evaluated: differences between adolescents and adults in nicotine's behavioral effects. We reported previously that (1) chronically administered nicotine (via osmotic minipump) had greater activity-stimulating effects in adolescent male rats than in adult male rats (Faraday et al., 2001); (2) adolescent and adult male rats exhibited different dose–response curves to acutely administered nicotine, with peak activity for adults at 0.50 mg/kg and peak activity for adolescents at both 0.50 and 1.0 mg/kg (Faraday et al., 2003a); and (3) adolescent rats were relatively insensitive to nicotine's activity-decreasing effects at low and high dosages (Faraday et al., 2003a). These findings suggest that adolescents may differ from adults in activity effects of nicotine.

It also is possible that adolescents differ from adults in terms of nicotine's anxiolytic effects, but this question has not been thoroughly evaluated. One study has examined nicotine's effects in the social interaction test. Cheetah et al. (2001) reported that nicotine was anxio-

☆ The opinions or assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Department of Defense or the Uniformed Services University of the Health Sciences.

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0091-3057/$ – see front matter © 2003 Elsevier Inc. All rights reserved.
doi:10.1016/j.pbb.2003.09.016

lytic (i.e., increased social interaction) at low nicotine dosages (0.05 and 0.10 mg/kg) for adolescent females and at higher nicotine dosages (0.25 mg/kg) for adolescent males. These data suggest that there are gender differences in sensitivity to nicotine's anxiolytic actions among adolescents. However, this study did not include an adult comparison group. It is unclear, therefore, whether there are age differences in nicotine's anxiolytic actions. In addition, the responses of adult males and females to the effects of nicotine generally have not been compared.

In studies of adult male animals, nicotine has been reported to have no effect on anxiety-related behaviors (Balfour et al., 1986a,b; Benwell et al., 1994), to exert anxiolytic effects (Brioni et al., 1993; Onaivi et al., 1994; Vale and Green, 1996; Irvine et al., 2001), or to exert anxiogenic effects (Irvine et al., 2001). There are a number of possible reasons for these conflicting findings, including different methods of assessing anxiety (e.g., social interaction vs. elevated plus maze [EPM]), different nicotine doses and dosing regimens, and different strains of animals.

The present experiment had two purposes: (1) to evaluate possible age and gender differences in nicotine's effects on a widely used behavioral measure of anxiety—the EPM and (2) to attempt to replicate our previous activity findings in adult and adolescent males and to extend these findings to females.

2. Methods

2.1. Subjects and housing

Subjects were 160 Sprague–Dawley rats (80 male and 80 female). Within each sex, half of the animals were adolescent (30 days old at the beginning of the experiment) and half were adult (60 days old at the beginning of the experiment). Same-age, same-sex animals were pair-housed in standard polypropylene shoebox cages (42 × 20.5 × 20 cm) on hardwood chip bedding (Pine-Dri). Throughout the study, animals had continuous access to rodent chow (Teklad 4% Mouse/Rat Diet 7001) and water. The housing room was maintained at 23 °C and 50% relative humidity on a 12-h reversed light/dark cycle (lights on at 1700 h). The experiment was conducted as a 2 (male or female) × 2 (adult or adolescent) × 4 (saline, 0.10, 0.50, or 1.0 mg/kg nicotine) full factorial design, with 10 subjects per treatment cell. Adolescence was defined as the period spanning 28–42 days (Spear, 2000). This experimental protocol was approved by the USUHS Institutional Animal Care and Use Committee and was conducted in full compliance with the National Institutes of Health Guide for Care and Use of Laboratory Animals (NIH Pub. 82-23, rev. 1985).

2.2. Equipment

2.2.1. Locomotor activity

Locomotor activity was measured using an Omnitech Electronics Digispan infrared photocell system (test box model RXYZCM [16 TAO]; Omnitech Electronics, Columbus, OH) located in a dedicated room. This room is constructed of cinderblock walls, acoustic tile ceiling, and steel doors so that outside sound is kept to a minimum. Animals were placed in a 40 × 40 × 30-cm clear Plexiglas arena. A Plexiglas lid with multiple 3.5-cm-diameter ventilation holes was placed on top of the arena. A photocell array measured horizontal locomotor activity using 16 pairs of infrared photocells located every 2.5 cm from side-to-side and 16 pairs of infrared photocells located front-to-back in a plane 2 cm above the floor of the arena. Data were automatically gathered and transmitted to a computer via an Omnitech Model DCM-I-BBU analyzer. The apparatus monitored animal activity continuously with data recorded as cumulative activity every 5 min for a total testing period of 1 h. All animals were placed in the testing chambers immediately following injections. Cage mates were always removed from the cage within 30 s of one another and tested at the same time (in separate chambers) to avoid any within-cage order effects. Once subjects were placed in the test arenas, the experimenter turned off the lights and left subjects undisturbed during the testing period. Testing arenas were cleaned with 50% ethanol solution between subjects.

2.2.2. Elevated plus maze

The EPM is a widely used measure of anxiety (Lister, 1990; Hogg, 1996). The EPM is shaped like a plus sign and consists of a square platform (10 × 10 cm), with four arms (45 × 10 cm) radiating out from the center platform elevated to a height of 50 cm above the floor. The center platform and arms are made of smooth plywood, painted black. Two arms are "open" (no walls) and two arms are "closed" (45 × 50 × 0.5 cm covered with opaque black Plexiglas). The only illumination in the room came from a single 60-W bulb aimed at the ceiling directly above the maze.

Rats were placed individually on the center platform facing a closed arm and allowed to explore the maze for 5 min. Behaviors were videotaped via closed circuit TV camera for later scoring by two scorers. Behaviors scored included: percent time spent in the open arms [(time spent in open arms/total time) × 100], percentage of open arms entries [(open arm entries/total arm entries) × 100], and percentage of closed arm entries [(closed arm entries/total arm entries) × 100]. Percent time spent in the open arms and percentage of open arm entries were chosen to index anxiety because these behaviors repeatedly correlate with anxiety (Ferandes and File, 1996; Hogg, 1996; Rodgers and Dalvi, 1997). These parameters have been validated both pharmacologically and behaviorally. Specifically, anxiogenic drugs

decrease these parameters, anxiolytic drugs increase these parameters, and animals confined to the open arms exhibit more fear responses than animals confined to closed arms (Ferandes and File, 1996; Rodgers and Dalvi, 1997; Pellow et al., 1985). To ensure that behavior in the maze did not simply reflect changes in activity, percent closed arms entries also were scored. This parameter is reportedly the purest measure of locomotor activity on the elevated-plus maze (Ferandes and File, 1996; Hogg, 1996). The maze floor and walls were wiped clean with 50% ethanol following each animal.

In this study, we measured locomotor activity 24 h before and 24 h after EPM, purposely allowing a 24-h gap between locomotor testing and EPM testing. The primary focus of the study was to determine whether there were age and gender differences in nicotine's effects on anxiety. It was necessary to measure locomotor activity to ensure that changes in EPM performance could not be attributed to nicotine's effects on activity.

Previous investigators have cautioned against testing animals on other measures immediately prior to EPM experience (Hogg, 1996; Pellow et al., 1985). Other investigators have measured EPM after locomotor and other behavioral tests and reported clear findings (Lister, 1987; Ferandes and File, 1996). In this study, by purposely spreading out the measures across 24-h, the authors were able to both maximize the relevance of the locomotor data and minimize the effects of prior locomotor testing on subsequent EPM responses. We are not aware of any other studies that have used this paradigm and found this time span (i.e., 24-h) to alter EPM responses. Therefore, the authors believe that this testing schedule, especially the 24-h gap between locomotor and EPM, is unlikely to have affected subsequent EPM responses.

2.3. Drug administration

Nicotine (0.1, 0.5, or 1.0 mg/kg) or physiologic saline was administered via subcutaneous injections between the shoulder blades. These dosages were selected to span those commonly used in the literature. Physiological saline also was used as a vehicle for the nicotine solution. Solutions were pH adjusted to physiologic saline pH using Na_2PO_4. Nicotine solution was made from nicotine dihydrochloride (MW = 235.13) and is expressed as nicotine base. All injections were in volumes of 1 ml/kg.

2.4. Procedure

The procedure included two phases: a predrug baseline/acclimation phase and a drug administration phase.

2.4.1. Baseline/acclimation phase

Subjects were handled for a few minutes once each day for 2 days to minimize any stress that might occur as a result of necessary handling for injections. Animal body weights also were measured during this period for the purpose of balancing experimental groups. The baseline phase spanned ages 25–30 days for adolescents and 55–60 days for adults.

2.4.2. Drug administration phase (5 days)

After the completion of baseline measures, subjects were assigned within age and sex to drug groups (saline, 0.10, 0.50, or 1.0 mg/kg nicotine) in a manner that assured comparable, initial body weights. Activity was measured on Drug Days 1, 3, and 5. EPM behaviors were measured on Drug Day 2. Both activity and EPM testing were conducted during the dark or active portion of the cycle (lights on at 1700 h).

2.5. Data analytic strategy

Horizontal activity data were analyzed using separate repeated-measures analyses of variance (ANOVAs) with a within-subjects factor of day and between-subjects factors of age, gender, and drug. ANOVAs were used to assess for effects of age, gender, and drug on specific days. Although there were age differences in overall baseline activity, running the analyses with baseline as a covariate did not significantly alter the resulting drug effects. Therefore, to account for this baseline difference, the effects of nicotine also were analyzed within both age groups. For EPM, the percentage of open arm entries relative to the total, the percentage of time that animals spent in the open arms, and percent closed arm entries were analyzed using multivariate ANOVAs (MANOVAs) with factors of age, sex, and drug. Animals that fell off the maze prior to the completion of the 5-min testing period were excluded from the analyses. A total of eight animals fell off of the maze (adolescent females: one saline, two 0.5 m/kg; adolescent males: one saline, one 1.0 mg/kg; adult females: one 0.5 mg/kg; adult males: one saline, one 0.5 mg/kg). Data also were examined within each age group for effects of sex and drug. All tests were two-tailed. Results are significant at $P < .05$ unless otherwise noted. Trends (i.e., P values greater than .05) are reported where they are part of an overall pattern of significant effects. Tukey's HSD post hoc tests were used to determine differences among drug groups. At every level of analysis (e.g., when all animals were considered together, when age groups were considered separately), activity rose significantly over time (effect of day). These effects are not reported.

The order in which the results are presented is intended to highlight the primary question of the current study. That is, are there age and gender differences in nicotine's anxiolytic effects? EPM data are presented first because the EPM was the measure selected to answer this question. Further, no previous studies have examined age and gender differences in nicotine's effects on the EPM. Therefore, the EPM findings represent the newest and most significant contribution to the existing literature. Locomotor activity data were included as a separate measure primarily to ensure

that behavior on the EPM could not be attributed to nicotine's known effects on activity. Locomotor data follow the EPM results because they were included to support EPM findings.

3. Results

3.1. Elevated plus maze

3.1.1. Percentage of time in open arms

Increases in percentage time in open arms are interpreted as evidence of anxiolysis (see Fig. 1a) (Ferandes and File, 1996; Hogg, 1996; Rodgers and Dalvi, 1997). When all animals were considered together, adolescents spent more time in the open arms than did adults [age: $F(1,136)=36.70$]. Nicotine-treated animals generally spent less time in the open arms than did saline-treated controls [drug: $F(3,136)=3.64$] but these effects depended on age [age × drug: $F(3,136)=5.47$] and gender [age × drug × gender: $F(3,136)=3.63$]. Specifically, among adults, nicotine reduced percentage of time spent in the open arms [$F(3,69)=8.56$] with all groups spending significantly less time in the open arms than the saline group. These decreases also were evident when adult males and females were examined separately [adult males: $F(3,34)=4.24$; adult females: $F(3,35)=6.01$], but males and females differed in dose–response effects of nicotine with 0.10 mg/kg reducing percentage of time in open arms for males and all nicotine groups spending less time in the open than the saline group for females.

Among adolescents, nicotine (0.5 and 1.0 mg/kg) increased percent time in the open arms for males, but decreased this parameter for females [drug × gender: $F(3,67)=11.32$]. These differences were significant when adolescent males and females were examined separately [adolescent males: $F(3,34)=8.13$; adolescent females: $F(3,33)=3.75$].

3.1.2. Percentage of open arm entries

Increases in percentage of open arm entries can be interpreted as evidence of anxiolysis but also may reflect

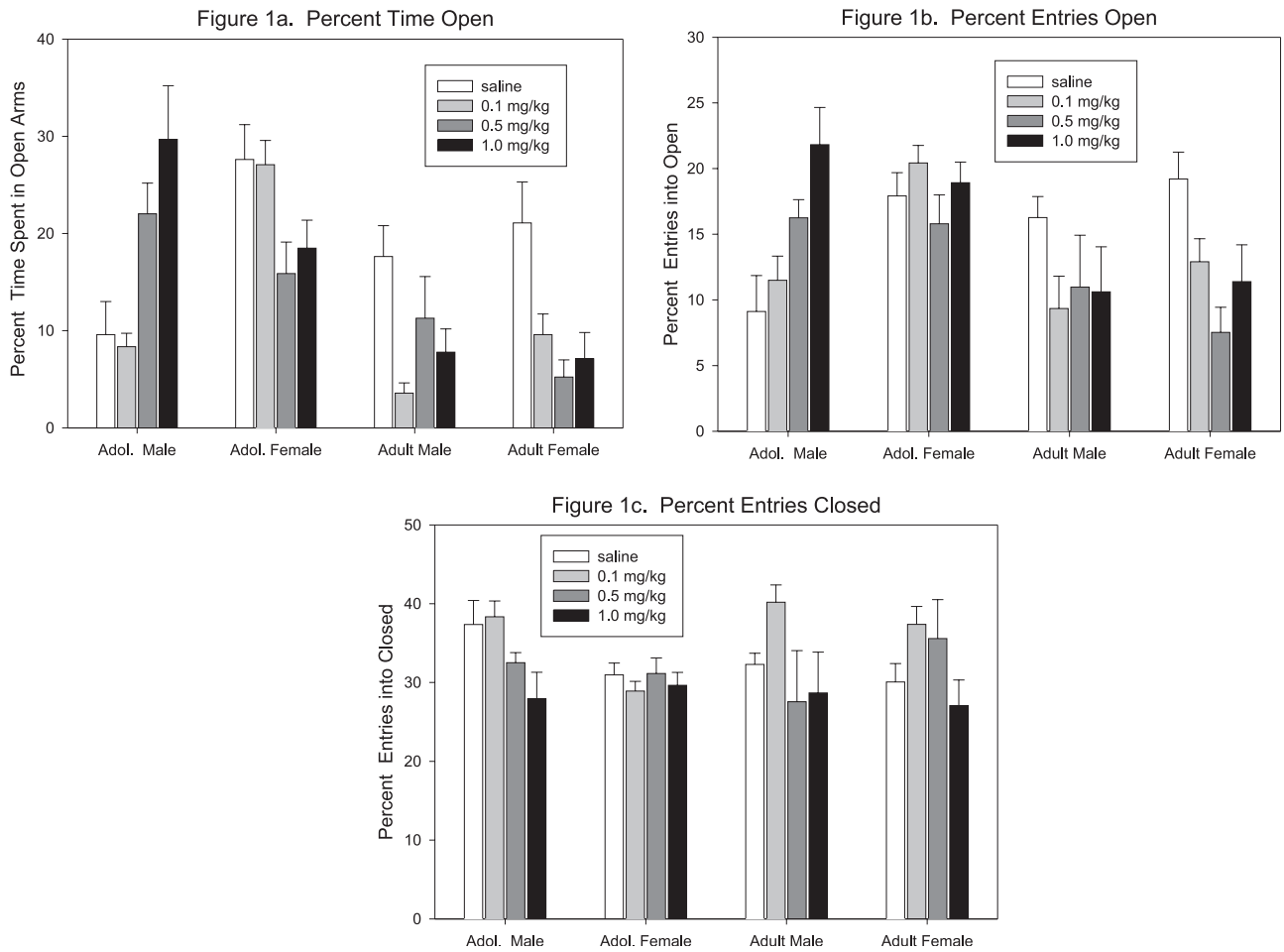

Fig. 1. (a) Percent time spent in open arms (time spent in open arms/total time spent on maze) over 5 min (group means ± S.E.M.) for all animals during the drug phase. (b) Percent entries into open arms (entries into open arms/total entries into all arms) over 5 min (group means ± S.E.M.) for all animals during the drug phase. (c) Percent entries into closed arms (entries into closed arms/total entries into all arms) over 5 min (group means ± S.E.M.) for all animals during the drug phase.

exploration because this measure depends on the number of times an animal moves back and forth between the closed and open arms (see Fig. 1b) (Ferandes and File, 1996; Hogg, 1996). When all animals were analyzed together, adolescents made a greater percentage of open arm entries than did adults [age: $F(1,136)=12.87$]. Effects of nicotine depended on age [Age × Drug; $F(3,136)=6.33$] and gender [Gender × Drug: $F(3,136)=3.53$]. Within adolescents, females had a greater percentage of open arm entries [gender: $F(1,67)=6.54$] than did males. Nicotine increased percentage of open arm entries in adolescent males but not in adolescent females [Drug × Gender: $F(3,67)=4.85$]. For adolescent males, the 1.0-mg/kg group exhibited greater percentage open arm entries than did the saline group [$F(3,35)=6.13$].

Within adults, nicotine reduced the percentage of open arm entries with all groups differing significantly from saline [$F(3,69)=4.00$]. There were no effects of gender or Gender × Drug interactions.

3.1.3. Percent closed arm entries

Percent closed arm entries is interpreted as evidence of general activity (see Fig. 1c) (Ferandes and File, 1996; Hogg, 1996). When all animals were analyzed together, nicotine generally decreased the percentage of closed arm entries [$F(3,136)=4.51$]. Although there were no main effects for gender or age or interactions, data were further analyzed within age and sex to parallel the previous analytic strategy. Within adolescent males, nicotine decreased the total number of closed arm entries [$F(3,34)=3.65$] at the 1.0-mg/kg dose only. Nicotine did not significantly affect closed arm entries in adolescent females or in adult rats.

3.1.4. Activity

Nicotine altered activity levels [drug: $F(3,144)=50.97$] and these effects grew larger over drug days [Day × Drug $F(6,288)=12.49$] and depended on gender [Drug × Gender: $F(3,144)=3.83$] and age [Time × Age × Drug: $F(6,288)=4.13$; Age × Drug: $F(3,144)=11.21$] (see Fig. 2a–d). Females generally were more active than males [gender: $F(1,144)=70.94$].

Because of the overall age differences in locomotor activity and because the effects of nicotine differed depending on age, the effects of nicotine also were examined separately for adults and adolescents. Nicotine altered activity [adolescents: drug: $F(3,72)=46.68$; adults: drug: $F(3,72)=19.56$] and these effects grew larger over drug days [adolescents: Day × Drug: $F(6,144)=5.48$; adults: Day × Drug: $F(6,144)=10.88$]. For both age groups, females were more active than were males [adolescents: $F(1,72)=29.42$; adults: $F(1,72)=41.53$]. Dose–response patterns differed, however, based on age. Among adults,

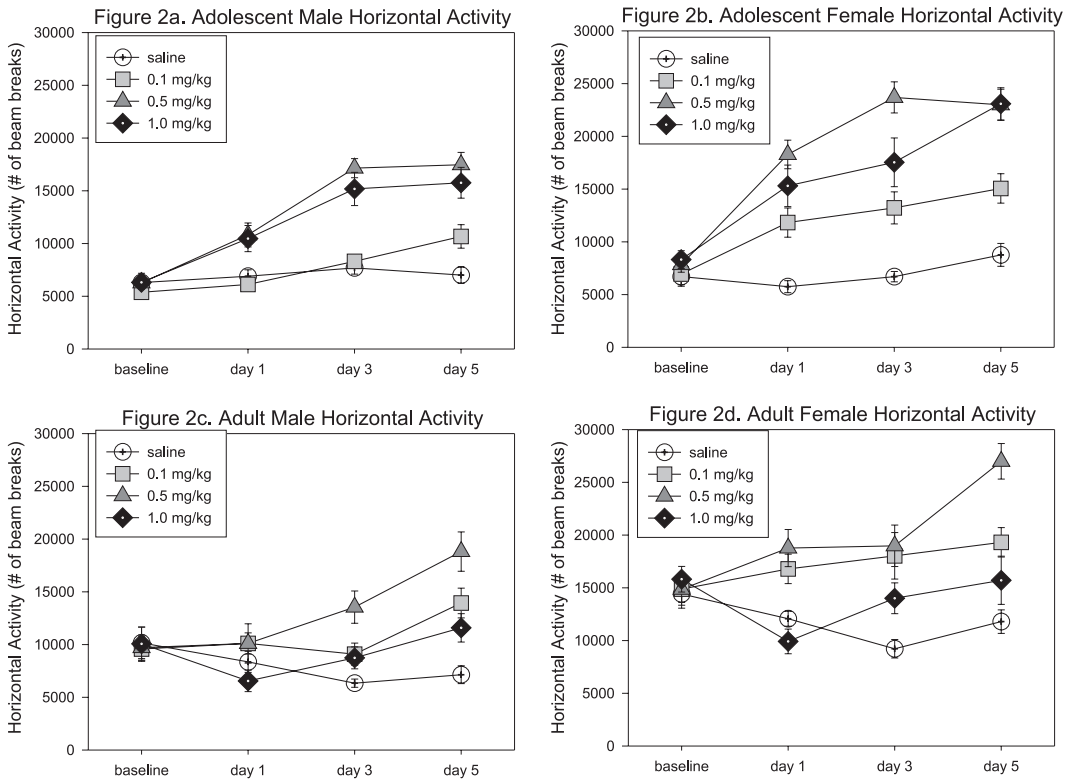

Fig. 2. (a) Open-field activity (number of beam breaks) during 5-min periods over 1 h (group means ± S.E.M.) during drug phase for adolescent males. (b) Open-field activity (number of beam breaks) during 5-min periods over 1 h (group means ± S.E.M.) during drug phase for adolescent females. (c) Open-field activity (number of beam breaks) during 5-min periods over 1 h (group means ± S.E.M.) during drug phase for adult males. (d) Open-field activity (number of beam breaks) during 5-min periods over 1 h (group means ± S.E.M.) during drug phase for adult females.

on average peak activity occurred at the 0.50-mg/kg dosage, and the 1.0-mg/kg group did not differ significantly from saline. In contrast, for adolescents the 1.0- and 0.5-mg/kg dosages produced similar activity levels and all nicotine groups exhibited greater activity levels than did the saline group. In addition, for adolescents, but not for adults, there were gender differences in nicotine's effects [adolescents: Gender × Drug: $F(3,72) = 3.73$].

For both adolescent males and females, nicotine altered activity [males: drug: $F(3,36) = 23.68$; females: drug: $F(3,36) = 25.83$] and these effects grew larger over drug days [males: Day × Drug: $F(6,72) = 4.36$; females: Day × Drug: $F(6,72) = 3.12$]. For males, on average, the 0.5- and 1.0-mg/kg dosages increased activity significantly compared to saline. These differences also were evident when data from each drug day were considered separately. For females, all drug groups exhibited greater activity levels compared to saline. Similarly, data from each drug day revealed the same patterns.

For both adult males and females, nicotine increased activity levels over the drug administration period [males: drug: $F(3,36) = 7.66$; females: drug: $F(3,36) = 11.99$] and these effects grew larger over time [males: Day × Drug: $F(2,72) = 6.76$; females: Day × Drug: $F(3,36) = 5.92$]. For males, on average, only the 0.5-mg/kg group was more active than the saline group. When each day was examined separately, the 0.5-mg/kg group was more active than the saline group on Drug Day 3, and both the 0.1- and 0.5-mg/kg groups were more active than the saline group on Drug Day 5. For females, the 0.1- and 0.5-mg/kg groups were more active than the saline group on average and these differences were present on each drug day.

4. Discussion

This experiment examined the effects of repeated–acute nicotine administration (saline, 0.1, 0.5, or 1.0 mg/kg daily) on EPM and locomotor behaviors of adolescent and adult male and female rats. Nicotine's effects depended on age and sex of animal.

4.1. Elevated plus maze

Nicotine exerted anxiolytic effects (increased percentage of time in the open arms) in adolescent males but exerted anxiogenic effects (decreased percentage of time in the open arms) in adolescent females and in adult males and females. This pattern generally was evident when percentage of entries into open arms was considered. Importantly, these effects were not the result of nicotine's activity-altering actions. That is, nicotine's effects on percentage of entries into closed arms (a measure of activity) for each group did not parallel effects on percentage of time in the open arms.

Findings for adolescents are consistent with the report of Cheetah et al. (2001) in that there were sex differences among adolescents. Using the social interaction test to evaluate anxiety, these investigators reported that females were more sensitive to nicotine's anxiolytic actions than were males. In the present experiment, the reverse relationship was detected: adolescent males were more sensitive to nicotine's anxiolytic actions and nicotine was anxiogenic for adolescent females. Nicotine dosage may be relevant to these different findings because the dosage that produced anxiolytic effects in females was lower (0.05 mg/kg) in Cheetah et al. (2001) than the lowest dosage used in the present experiment. Rat strain also may be a variable in the differences—Cheetah et al. (2001) used Lister rats and we used Sprague–Dawley rats. We have previously reported strain differences in nicotine's behavioral effects (Faraday et al., 2003b). It also is possible that these differing results were obtained because the EPM and the social interaction test index different types or aspects of anxiety. For example, the social interaction test has been interpreted to model generalized anxiety, whereas the EPM has been interpreted to model panic disorder (File et al., 2000).

In adult male Sprague–Dawleys, Benwell et al. (1994) reported that nicotine had no effect on EPM behaviors. The dosing procedures in that experiment, however, differed substantially from those used in the present experiment in which we detected anxiogenesis in adult males as well as females. In Benwell et al. (1994), animals were administered 0.4 mg/kg day nicotine via osmotic minipump for 14 days and additional nicotine (0.4 mg/kg) was administered by acute injection on drug administration Days 9–13; EPM behaviors were evaluated on drug administration Day 14. Other reports of no nicotine effects (Balfour et al., 1986a,b) also used markedly different dosing and testing procedures (e.g., tested animals for 20 min). In the current study, EPM behavior was observed for 5 min, 10 min following an injection of nicotine (0.1, 0.5, or 1.0 mg/kg) or saline.

Onaivi et al. (1994) reported that nicotine exerted anxiolytic effects on EPM behaviors in adult Fischer-344 male rats. In this study, nicotine was administered via drinking water and the anxiolytic effects occurred in aged rats (24+ months old) but not in young adult rats (90 days old). Irvine et al. (2001) also reported that nicotine was anxiolytic in the EPM, but only after 7 days of injections. In this study, nicotine was anxiogenic when EPM testing occurred 30 min after injection (Irvine et al., 2001). These findings suggest that nicotine's effects on anxiety may depend on timing with anxiogenic effects occurring after acute administration and anxiolytic effects occurring only after repeated exposure to nicotine. The current finding that nicotine is anxiogenic in females and adult males is consistent with these previous reports.

Although some investigators have cautioned against behavioral testing conducted prior to EPM (Pellow et al., 1985; Hogg, 1996), prior testing cannot fully explain the current results because exposure was the same for all groups and age differences in nicotine's effects were still present. Even if prior handling does affect subsequent EPM re-

sponse, then age and gender are variables relevant to nicotine's behavioral actions.

4.2. Locomotor activity

Locomotor activity was included primarily to ensure that nicotine's effects on EPM could not be attributed to nicotine's activity effects. Nicotine's repeated–acute effects differed in adolescent and adult rats. For adolescents, peak activity levels occurred at the 1.0-mg/kg dosages and nicotine accounted for 66% of overall activity variance ($\eta^2 = 0.660$). For adults, peak activity occurred at the 0.5-mg/kg dosage and nicotine accounted for 45% of activity variance ($\eta^2 = 0.449$). Further, among adults, the 1.0-mg/kg dosage reduced activity below the saline level on Day 1 and below the 0.5-mg/kg level on Days 1, 3, and 5. These activity-decreasing effects were not present among adolescents, suggesting that adolescents are less sensitive to nicotine's depressant actions. The finding that adolescents and adults differ in their peak response to nicotine's actions and the absence of depressant effects in adolescent rats replicate our previous findings in male adolescent and adult rats (Faraday et al., 2003a).

It is worth noting that the activity effects of nicotine in the locomotion chamber differed from nicotine's activity effects in the EPM. For example, 0.50 and 1.0 mg/kg increased activity of adolescent males in the locomotion chamber but decreased activity in the EPM (percent entries closed). The same nicotine dosages increased adolescent female activity in the locomotion chamber but had no effect on activity in the EPM. Among adults, nicotine effects in the locomotion chamber also did not parallel nicotine effects on activity in the EPM. These data indicate the sensitivity of nicotine's activity effects to the environment in which activity is measured. These data also are consistent with our report that nicotine's activity effects differ between the locomotion chamber and the home cage (Faraday et al., 2003a).

4.3. Summary and implications

Findings from the present experiment suggest that nicotine's actions differ based on age and gender. In particular, these findings suggest that adolescent males are more sensitive to nicotine's anxiety-relieving effects than are adolescent females or adult males and females. The complexity of the nicotine-anxiety literature suggests, however, that these effects may depend on the context in which anxiety occurs. In particular, the EPM is a situation in which the animal is alone in a stressful or novel environment. If these findings extrapolate to humans, then they suggest that nicotine may have anxiety-relieving properties for young male smokers in this type of environment. The findings of Cheetah et al. (2001), in which anxiety was assessed in a social situation, suggest that nicotine might be anxiolytic for young female smokers in social environments.

There is an alternative interpretation of Cheetah et al. (2001) findings. One of the female (human and animal) behavioral responses to stressful situations is to affiliate (Taylor et al., 2000). Therefore, females may interact in the social interaction test because they are anxious rather than because they are not anxious. Therefore, it is possible that nicotine was anxiogenic in both behavioral tests of anxiety for adolescent females. If so, human adolescent females may not obtain anxiolytic effects from nicotine despite reports that young women smoke to manage affect. We have found a similar disparity between reported reasons for smoking and actual nicotine effects in experiments examining nicotine's body weight- and appetite-reducing effects in adolescent and adult males and females (Faraday et al., 2001). In this study, we found that nicotine (chronically administered) reduced feeding and body weight in adolescent males and in adult males and females, but did not reduce feeding and body weight in adolescent females. These results contrast with reports by adolescent girls that they smoke to reduce appetite and body weight and may indicate that nicotine's appetite- and body weight-reducing effects do not occur until adulthood. Smoking initiation and maintenance by adolescent girls, therefore, may be based on inaccurate perceptions of how nicotine will affect them. If the results from the current study extend to humans, then challenging these inaccurate perceptions in adolescents may be the key to early intervention and prevention.

Acknowledgements

This work was supported by Robert Wood Johnson Grant No. 036413. The authors thank Virginia Minich, Amy Hein, and Sara Mixter for their technical assistance.

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